

The claims have been rejected for allegedly being unpatentable over Priebe (U.S. Patent No. 5,625,043) in combination with Piazza et al (U.S. Patent No. 5,858,694). Applicants respectfully request reconsideration because the present invention is unexpected from the teachings of either reference alone or taken together.

The Examiner has asserted that one in the art would have expected the resulting combination of the present invention to be useful in treating neoplastic tumors.

Applicants respectfully submit that such a position would essentially render any combination of cancer treatment regimens unpatentable. That position flies in the face of the countless combinations that are untenable for use because, for example, the resulting adverse side-effects from the drug combination add to each other and sickens the patient beyond relief. Thus, merely two drugs being in the same field of cancer-treatment, without more, would not lead one to expect their combined usefulness.

As pointed out in the original specification at page 35 lines 17-27, the side-effects of a cGMP-specific PDE inhibitor and the side-effects of anthracycline antibiotics unexpectedly do not overlap. One affects the liver enzymes, while the other affects the myocardial system. Priebe and Piazza, taken alone or together, do not suggest, teach, or motivate that such non-overlapping side-effects would fortunately allow for the two drugs' use at their individual therapeutic doses – resulting in the addition of their therapeutic effects without any resulting addition of their adverse non-therapeutic effects.

Applicants respectfully submit that such results are completely surprising in light of the art. Thus, the rejection has been overcome, the application is in condition for allowance, and Applicants respectfully request a Notice to that effect.

#### Information Disclosure Statement

The Examiner noted that the references submitted in the Information Disclosure Statement (IDS) on September 4, 2002 were not received by the Examiner. Applicants respectfully enclose a copy of that IDS, together with copies of the foreign patent publications and scientific publications. Copies of the U.S. Patents are not enclosed as they should not be sent according to present PTO practice. Further, Applicants respectfully request that foreign language patent publication No. EP 0 722 943 be replaced with its equivalent U.S. Patent No. 5,866,571 issued February 2, 1999; EP 0 722

944 with its equivalent U.S. Patent No. 5,861,404 issued January 19, 1999; EP 1 074 258 with its equivalent U.S. Patent Publication No. 200201199 published August 29, 2002; WO 00/12501 with its equivalent U.S. Patent No. 6,436,952 issued August 20, 2002; WO 00/26201 with its equivalent U.S. Patent No. 6,376,493 issued April 23, 2002; WO 99/65880 with its equivalent U.S. Patent No. 6,417,188 issued July 9, 2002; WO 98/17668 with its equivalent U.S. Patent No. 6,130,223 issued October 10, 2000; WO 98/14448 with its equivalent U.S. Patent No. 6,265,577 issued July 24, 2001; WO 98/06722 with its equivalent U.S. Patent No. 6,110,920 issued August 29, 2000; WO 97/24334 with its equivalent U.S. Patent No. 6,166,219 issued December 26, 2000.

Accordingly, the above foreign language publications have been omitted and their U.S. equivalent patents have been noted on the enclosed copy of the previously submitted form 1449. Further, Applicants respectfully enclose a copy of the return postcard from the previously submitted IDS, which indicates that the PTO received the IDS with its cited references and the required Form 1449. Applicants respectfully request entry of the IDS and the Examiner's acknowledgement of the references by initially the Form 1449 appropriately.

Attorney for Applicants can be reached at the telephone number and address below. Commissioner is authorized to charge any deficiencies and credit any overpayment to OSI Pharmaceuticals, Inc. Deposit Account No. **502783**.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date appearing below.

OSI PHARMACEUTICALS, Inc.  
By Shu M. Lee Date 17 Nov 2003

Very truly yours,



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